

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 2 and 3 have been cancelled without prejudice and replaced with new claims 16-18, and claims 4, 5, 8, 12 and 13 have been amended. The changes to the claims have been effected to more particularly define the present invention and to put the claims in better form under U.S. practice. Support the claim amendments and new claims is readily apparent from the teachings of the specification and the original claims.

Applicants wish to note that the current pending claims (prior to this amendment) are claims 2-15 and not claims 2-14 as noted in the May 31, 2002 Action. Applicants believe that the Examiner has inadvertently omitted non-elected claim 15 from the pending claims. Applicants request the Examiner to correct this oversight in the next Official Action.

With regard to the rejection of claims 2-7, 12 and 13 under 35 USC § 112, first paragraph, on new matter grounds, this rejection has been rendered moot by the deletion of the rejected limitation (i.e. *"provided that a combination wherein R⁷ is methyl, R⁸ is methyl and R⁹ is methyl is excluded"*) from the claims.

With regard to the rejection of claims 2-7, 12 and 13 under 35 USC § 112, first paragraph, on enablement grounds, this rejection is deemed to be untenable and is thus respectfully traversed.

The Examiner points out by referring to the documents, Dickens et al., (WO 94/02447), Brenner (WO 97/05865) and Crimmin et al. (USP 5,652,262), that this area (in connection with MMP inhibitor) is highly unpredictable and alteration of the compounds results in altered activities and altered formulation profiles which have entirely unpredictable results. Thus, the Examiner believes that undue experimentation would be required to practice the claimed invention even though the specification provides substantial guidance on methods of making the claimed compounds and on the use of such

compounds (see the working examples in the specification, particularly the 40 or so compounds disclosed in Tables 1-3 on pages 148-152 of the specification).

Applicants strongly disagree with the Examiner's conclusions in this regard. It is noted that the reference, Chemical Reviews, Vol. 99, No. 9, pp. 2735 to 2776 (1999) (see Appendix 2 enclosed herewith), discloses the summary of structure-activity relationships for right-hand side MMP inhibitors (see Figure 6 of the reference) wherein such MMP inhibitors correspond to the claimed compounds wherein $R^1 = R^2 = R^6 = H$.

Claimed Compounds of Formula (I)	Chemical Reviews, 99,2375-2776 (1999) Figure 6
R^1	H
R^2	H
R^3	R^a
R^4	R^1
R^5	H
R^6	R^3
$-C(R^7)(R^8)(R^9)$	R^2

In Figure 6 of the Chemical Reviews article, R^a (corresponding to R^3 as claimed) stands for unsubstituted or substituted alkyl or aralkyl and R^1 (corresponding to R^4 as claimed) also similarly does. Further, the term "Wide range of substituents tolerated" is noted for R^2 (corresponding to the moiety $-C(R^7)(R^8)(R^9)$ as claimed and R^3 (corresponding to R^6 as claimed), indicating a diversity of substituents.

Hence, it can be expected that such succinic acid-based compounds with a hydroxamic acid group would hold a stereoconfiguration formed by R^1 , R^2 and R^3 as illustrated in Figure 6 of the Chemical Reviews article, resulting in MMP inhibiting

activities as long as R¹, R² and R³ are not hydrogen, respectively.

As noted above, the instant claimed compounds meet the requirements for substituents as set forth in Figure 6 of the Chemical Reviews article. Accordingly, it can be expected that the instant claimed compounds would have MMP inhibiting activities.

As disclosed in Tables 1-3 on pages 148-152 of the specification and Appendix 3 (biological data, also enclosed herewith), the instant claimed compounds actually possess an MMP inhibiting activity.

In view of the foregoing remarks, Applicants believe that it is "predictable" and "expected" that not only the compounds with experimental biological data but also their analogues would have an MMP inhibiting activity. Applicants also believe that such MMP inhibiting activity can be determined without undue experimentation for the same reasons as noted above.

Thus, this rejection can no longer be sustained and should be withdrawn

With regard to the rejection of claims 2-7, 12 and 13 under 35 USC § 102(b) as being anticipated by Fujisawa et al. (JP 8-53403), this rejection is deemed to be untenable and is thus respectfully traversed.

Under U.S. practice, to constitute anticipation of the claimed invention, a single prior art reference must disclose each and every material element of the claim. Here, in this case, Fujisawa et al. fails to teach a material element of the claim since in compound (I) of Fujisawa et al., methyl is not included in the definition for R⁴.

Further, it should also be noted that the limitation of "provided that, when R¹ and R² are each hydrogen, R⁴ is 2-pyridyl or its N-oxide, or 4-pyridyl" is present (see column 1, lines 18 to 20 of Fujisawa et al.) in the definition of the Fujisawa et al. compound. Accordingly, in the compounds of Fujisawa et al., when R¹ and R² are each hydrogen, R⁴ is not phenyl. Also, since hydrogen has been deleted from the definition for "B" in the newly added claims, phenyl is not included for R⁹.

Thus, given the above distinctions, it is clear that the scope of the compounds of Fujisawa et al. does not overlap with that of the instantly claimed compounds.

As a result, this rejection also cannot be sustained and should be withdrawn.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

In view of the foregoing amendments and remarks, it is respectfully submitted that the Application is now in condition for allowance. Such action is thus respectfully solicited.

If, however, the Examiner has any suggestions for expediting allowance of the application or believes that direct communication with Applicants' attorney will advance the prosecution of this case, the Examiner is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

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